EXHIBIT 35

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Original Article

Effect of forced-air warming on the performance of operating theatre laminar flow ventilation*

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Summary

Forced-air warming exhaust may disrupt operating theatre airflows via formation of convection currents, which depends upon differences in exhaust and operating room air temperatures. We investigated whether the floor-to-ceiling temperatures around a draped manikin in a laminar-flow theatre differed when using three types of warming devices: a forced-air warming blanket (Bair Hugger™); an over-body conductive blanket (Hot Dog™); and an under-body resistive mattress (Inditherm™). With forced-air warming, mean (SD) temperatures were significantly elevated over the surgical site vs those measured with the conductive blanket (+2.73 (0.7) °C; $p < 0.001$) or resistive mattress (+3.63 (0.7) °C; $p < 0.001$). Air temperature differences were insignificant between devices at floor ($p = 0.339$), knee ($p = 0.799$) and head height levels ($p = 0.573$). We conclude that forced-air warming generates convection current activity in the vicinity of the surgical site. The clinical concern is that these currents may disrupt ventilation airflows intended to clear airborne contaminants from the surgical site.

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Patient warming systems are widely used to prevent unintentional peri-operative hypothermia based on the established benefits of reduced blood loss and transfusion [1], improved wound healing [2], reduced duration of hospital stay [3], improved survival [4] and reduced surgical site infection rates [5]. However, patient warming systems also release excess heat into the operating theatre that may generate convection currents even within a laminar flow system. It is possible that convection currents could disrupt the intended ceiling-to-floor theatre airflows and therefore impede the ventilation system's ability to clear contaminants from the surgical site.

There are two distinct categories of patient warming technology, forced-air and conductive heating. Forced-air devices deliver a heated airflow to a disposable coverlet that vents the hot air over the patient's body [6]. Conductive heating devices employ an electrically heated pad in contact with the patient's body [7]. Both types of devices appear to be comparably effective for the prevention of accidental peri-operative hypothermia [8–14], although forced-air devices are less efficient in transferring the applied heat to the patient than conductive devices [15]. Therefore, we might expect forced-air devices to generate a greater excess heat load on the ventilation system.

When considered in combination with other established sources of ventilation disruption such as surgical lights and personnel [16], even moderate changes in the excess heat load are of clinical importance. For example, convection currents due to forced-air warming occur in the vicinity of the surgical site. They are formed in the downstream 'wake' created by overhead lights and regions of blocked ventilation flow created by drapes and/or personnel. Convection currents were not observed when conductive patient warming devices were used [17]. McGovern et al. postulated that the observed disruption was due to excess heat as the result of patient warming excess heat, yet they made no measurements of ventilation field temperature nor did they establish the 'thermal' basis of such disruption.

Conceptually, the thermal basis of laminar flow disruption is the opposition of downward ventilation air currents by buoyancy-driven hot air convection currents. We assessed ventilation performance by measuring changes in ventilation field temperatures using a forced-air blanket (Bair Hugger™ 525; Arizant Healthcare Inc., Eden Prairie, MN, USA), with an over-body conductive blanket (Hot Dog™ B103; Augustine Temperature Management, Eden Prairie, MN, USA) and an under-body resistive mattress (Inditherm™ OTM1, Rotherham, UK) as controls. Our (null) hypothesis was that the use of forced-air warming would result in ventilation field temperatures similar to the conductive patient warming devices.

Methods

Experiments were conducted in a partial-walled ultraclean operating theatre (ExFlow 90, Howorth, UK; Validation certification QA ref AA719/1/SM) used for orthopaedic surgery (Royal Sussex County Hospital, UK). A manikin was placed in the supine position and a general surgical drape applied with the head end tented to form an anaesthesia screen (Fig. 1). The foot end of the drape was raised and folded over to create an air channel that directed the forced-air warming exhaust out of the ventilation field. A lower-body patient warming device (either the Bair Hugger, Hot Dog or Inditherm) was introduced under the drape (Fig. 2).

Ventilation field temperatures (Fig. 1) were measured floor-to-ceiling using 24 thermistors (KIMO KH200 Temperature and Humidity Loggers; Kimo, Montopon, France) placed across five heights:- floor (~5 cm above the floor); table (on the drape, ~60 cm from the floor); patient (2 cm above the dummy, ~80 cm from the floor); head (25 cm above the dummy, ~105 cm from the floor); ceiling (high level in the laminar flow, ~210 cm from the floor); and five locations (left shoulder, right shoulder, surgical site (abdomen), left knee, right knee); 24 locations resulted instead of 25 as it was not possible to measure the surgical site location at table height.

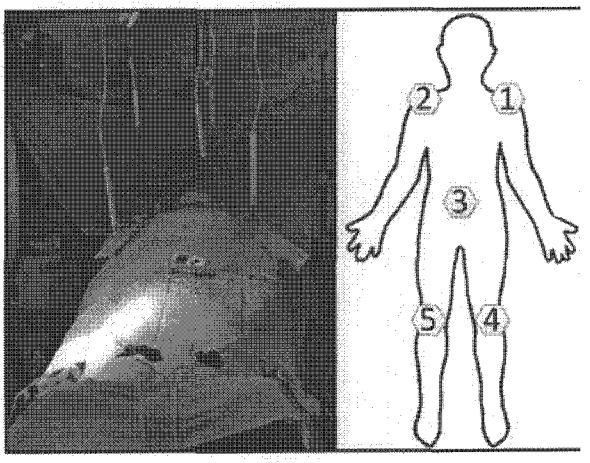

Figure 1 Manikin with raised foot drape and thermistors placed at 5 heights (floor, table, patient, head, overhead supply plenum) across five locations shown as (1) left shoulder; (2) right shoulder; (3) surgical site (abdomen); (4) left knee; and (5) right knee.

With each of the three patient warming devices, ventilation field temperatures were recorded at 60-s intervals for: (1) a 20-min 'control' period with the patient warming device turned off; (2) a 'transition' period of ~10 min when the patient warming device was turned on but had not thermally equilibrated with the ventilation environment; and (3) a 20-min 'steady-state' period when the patient warming device had thermally equilibrated and ventilation field temperatures had stabilised.

Air temperature differences from the overhead supply were computed by subtracting the time series of ventilation field temperatures at each location and height from the corresponding time series obtained at ceiling height for that location. Increases in air temperature were assessed as the average of this differenced time series for each location, height, time period

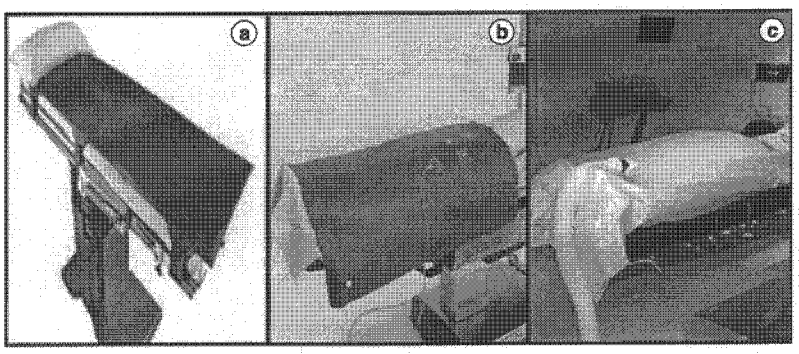

Figure 2 Patient warming devices evaluated: (a) under-body resistive mattress (Inditherm); (b) over-body conductive fabric blanket (Hot Dog); and (c) forced-air blanket (Bair Hugger).

(i.e. control, transition, steady state) and patient warming device.

Two separate classes of ANOVA models were fitted to the data. The first class assessed whether increases in air temperature were significantly different between patient warming devices when compared across control and steady-state periods for a given height. Formally, this difference between patient warming devices was assessed via the interaction term of an ANOVA model having 'increase in air temperature' as the response and 'blocking effects of period' (two levels: control and steady state) and 'environment' (three levels: forced-air warming run, conductive fabric run, and resistive mattress run) as the factors. Inclusion of a separate 'warming device' main effect in the model was not possible because it is perfectly correlated with the 'environment blocking term'. In other words, the main effect of warming device cannot be distinguished from, say, a 2 °C increase in overall environmental theatre temperature due to the time of day. Furthermore, we were interested in temperature increases by warming device for the steady-state period vs control period (which is the effect measured by the interaction term). The p value of interest is therefore the significance of the model interaction term when compared with an additive model using a log-likelihood ratio test.

A second class of ANOVA model was fitted to the temperature data for heights having a significant interaction term as described in the first model class. The purpose of this second model was to assess increase in air temperature vs control by location for a given height. Formally, an ANOVA model with interactions was fitted to the data for each significant height having increase in air temperature as the response and the following predictors: (1) 'environment blocking term' (three levels: forced-air run, conductive fabric run, and resistive mattress run); (2) 'location' (three levels: shoulder, surgical site which was always the abdomen, and knee); and (3) 'period' (two levels: control and steady state). It was necessary to pool the right and left measurements at the knee and shoulder locations to form replicates for inference. Means and standard errors are the maximum likelihood parameter estimates and p values were computed by applying t-tests to model parameter contrasts.

Results

Figure 3 shows an example of the temperature recordings obtained over the course of an experiment, with control, transition and steady-state periods highlighted.

The measured increase in air temperature vs control for each device by location and height (Fig. 4) showed forced-air warming to result in the greatest temperature increase at the patient height locations; for locations at the other heights (floor, table, head), there appeared to be no significant differences in air temperature between warming devices. This was confirmed by ANOVA; increases in steady-state air temperature vs control were significantly different between warming devices at the patient height ($p = 0.012$), but not at the other heights of floor ($p = 0.339$), table ($p = 0.799$) and head ($p = 0.573$).

A second class of ANOVA models was fitted to the patient height data to determine the specific effects of

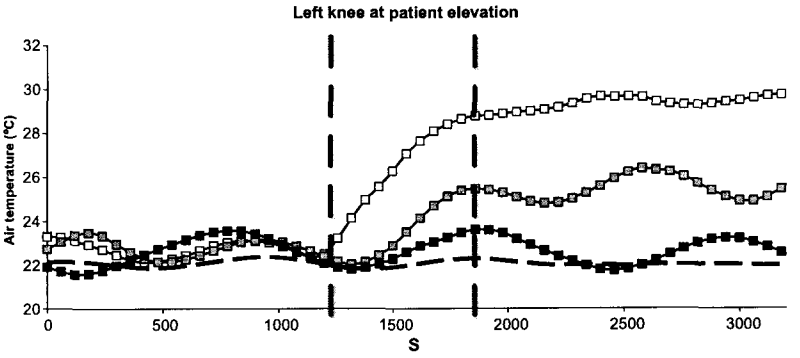

Figure 3 Absolute air temperature measurements for a single location (1 of 24) showing control period with patient warming device off (time = 0 to ~1200 s); transition period after turning device on (time = ~1200 s to ~1700 s) and steady state (from time = ~1700 s). Note the slightly varying temperature from the overhead supply. Temperature differences from the overhead supply were computed for the steady-state data and analysed for device comparisons. (-■-) resistive mattress, (-▨-) conductive blanket, (-□-) forced-air, (—) average overhead supply.

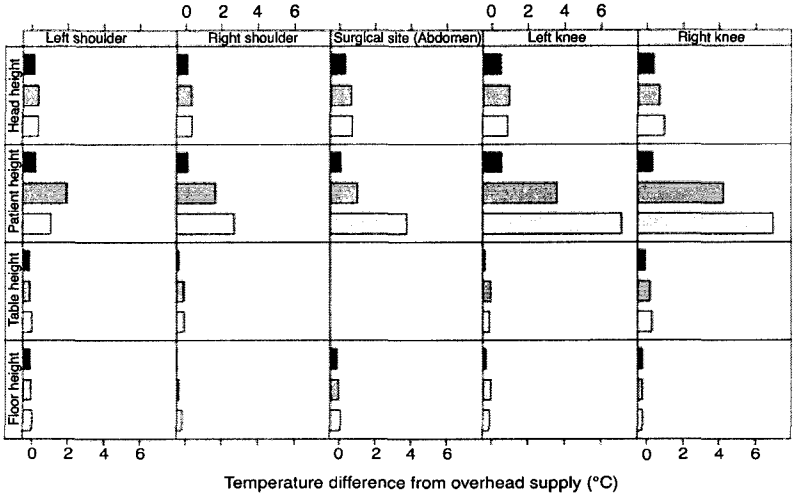

Figure 4 Steady-state increase in air temperature from the overhead supply for each patient warming device by location and elevation. (■) resistive mattress, (▨) conductive blanket, (□) forced-air

each patient warming device by location; these models were not applied to the floor, table, and head height data as there were no significant temperature differences vs control. There were significant differences in mean (SD) patient height air temperature vs control between warming devices at the locations of: knee, with forced-air 3.2 (0.5) °C ($p < 0.001$) higher than conductive fabric and 6.6 (0.5) °C ($p < 0.001$) higher than the resistive mattress; surgical site, with forced-air 2.7 (0.7) °C ($p < 0.001$) higher than conductive fabric and 3.6 (0.7) °C ($p < 0.001$) higher than the resistive mattress; and shoulder, with forced-air 1.7 (0.5) °C ($p = 0.01$) higher than resistive mattress. Differences were not significant between forced-air and conductive fabric at the shoulder location. Furthermore, conductive fabric air temperatures were significantly higher than the resistive mattress by 1.6 (0.5) °C ($p = 0.001$) and 3.5 (0.5) °C ($p < 0.001$) for the locations of shoulder and knee, respectively; these differences were not significant at the surgical site.

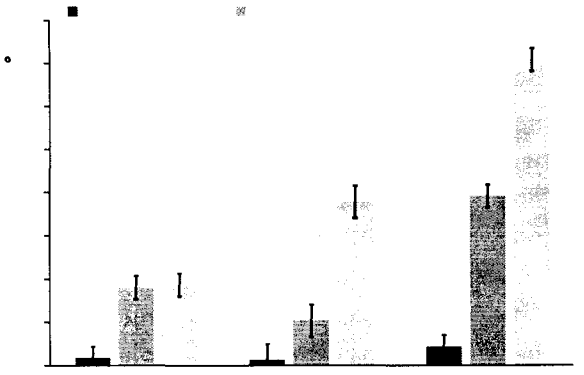

Figure 5 Average temperature increase from overhead supply at patient height by location. Right and left measurements for the shoulder and knee were pooled to allow for an estimate of dispersion. Error bars are SD.

Discussion

Our result rejects the null hypothesis, as we found forced-air warming to generate increased ventilation field temperatures vs both conductive warming devices. This finding suggests that forced-air warming technologies release significantly higher levels of excess heat than conductive warming technologies. Furthermore, forced-air warming temperature elevations were found to be the greatest above and around the surgical site. This finding is of concern because temperature elevations are the direct result of hot air-pockets moving upwards and against the downward laminar airflow currents. We can surmise this because air has a high transmissivity (i.e. low infrared absorption) [18]; thus, any temperature elevations are the result of convection current activity.

McGovern et al. used neutrally buoyant detergent bubbles released into theatre and found that forced-air warming appears to have a profound impact on laminar ventilation air-flows: there was large-scale dispersion of bubbles from the floor to the ceiling [17]. Our findings differ, in that we observed convection current activity directly above the patient and minimal activity elsewhere with forced-air warming. These differences could be due to the arrangement of the drapes; in our study, we raised the foot end of the drape to channel the forced-air warming exhaust outside the ventilation environment, whereas this channel was not present in the study of McGovern et al. in which the foot end of the drape extended to the floor. Therefore, the mass-flow of forced-air exhaust appears to play a critical role in the degree of ventilation disruption. Further studies are warranted to investigate whether specialised draping arrangements can lessen the risks of convection current formation. Both studies, however, confirmed that conductive warming technologies have little or no impact on ventilation airflows.

Although we attempted to mimic real conditions to a certain extent by having two people walk around within the laminar flow area, in a working operating theatre there are more people and many other ways by which the system might be disrupted [16, 17]. Another limitation of our study is that the definitive effects of this excess heat on clinical outcomes are presently unknown. Any future study might focus on particular types of surgery (e.g. that for device or joint implantation) where even small increases in airborne contamination are likely to be of more relevance [19]. Our findings may in part explain some aspects of the results of national studies over past 10 years, in which laminar flow ventilation has demonstrated either similar [20] or even higher [21, 22] infection rates than its conventional counterpart.

Balanced against these considerations, the prevention of hypothermia reduces the incidence of adverse events. Forced-air warming has been used on millions of patients and has been shown to be effective for managing unintended peri-operative hypothermia. The choice of warming device depends on a number of factors including the evidence base for the technology, cost, noise and even complaints from surgeons that they themselves become too warm [23]. Disruption of laminar flow should be one further objective factor guiding the proper choice.

Competing interests

Augustine Temperature Management loaned the Hot Dog conductive blanket and paid for the costs of temperature mapping. MA received paid support from Augustine Temperature Management for statistical analysis and manuscript preparation. No other external funding or competing interests declared.

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